Recommendations for initial treatment of chronic hepatitis B in nonpregnant adults

HBeAg	HBV DNA (PCR)	ALT	Treatment strategy
Patients without cirrhosis*			
+	>20,000 int. units/mL	≤2 x ULN¶	Treatment is not recommended because current treatment has low efficacy in inducing HBeAg seroconversion. Treatment may be considered in older patients (>40 years) and in those with family history of HCC.
			Patients should be monitored[Δ] and treatment considered if ALT becomes elevated >2 x ULN, liver biopsy shows moderate/severe inflammation or fibrosis[◇] (eg, METAVIR score ≥F2), and/or non-invasive testing suggests moderate/severe fibrosis.
+	>20,000 int. units/mL	>2 x ULN¶	Observe for 3 to 6 months if compensated and treat if no spontaneous HBeAg loss.
			Immediate treatment if icteric or clinical decompensation (eg, hepatitis B flare).
			ETV, TAF, TDF, or pegIFN-α are preferred for initial therapy.[§¥]
			End-point of treatment - Seroconversion from HBeAg to anti-HBe.[‡]
			Duration of therapy:
			▪ PegIFN-α: 48 weeks.
			▪ ETV, TAF, or TDF: Continue for at least 12 months after HBeAg seroconversion.
–	>2000 int. units/mL	>2 x ULN¶ OR 1 to 2 x ULN¶ if liver biopsy shows moderate/severe necroinflammation or significant fibrosis[◇] (eg, METAVIR score ≥F2) or non-invasive testing shows significant fibrosis	ETV, TAF, TDF, or pegIFN-α are preferred for initial therapy.[§¥]
			End-point of treatment - HBsAg loss.
			Duration of therapy:
			▪ pegIFN-α: One year.
			▪ ETV, TAF, or TDF: Several years or indefinite.[†]
–	≤2000 int. units/mL	≤ULN¶	Monitor and treat if HBV DNA and ALT increase as described above.
Patients with cirrhosis*			
+/–	Detectable	Any ALT	Compensated:
			▪ HBV DNA >2000 int. units/mL - Treat with ETV, TAF, or TDF.[§¥] Treatment should be continued indefinitely.**
			▪ HBV DNA <2000 int. units/mL - Consider treatment particularly if ALT elevated; close monitoring if treatment is not initiated.
			Decompensated:
			▪ Treat immediately, regardless of ALT or HBV DNA levels. ETV preferred.[§¥] TDF may be used with close monitoring of renal function. Refer for liver transplant.
+/–	Undetectable	Any ALT	Compensated: Observe.
			Decompensated: Refer for liver transplant, recheck HBV DNA during follow-up, evaluate for other causes of cirrhosis.

ALT: alanine aminotransferase; anti-HBe: antibody to hepatitis B e antigen; ETV: entecavir; HBeAg: Hepatitis B e antigen; HBsAg: hepatitis B surface antigen; HBV: hepatitis B virus; HCC: hepatocellular carcinoma; pegIFN-α: pegylated interferon alpha; TAF: tenofovir alafenamide; TDF: tenofovir disoproxil fumarate; ULN: upper limit of normal.

* Based upon findings on non-invasive testing or liver biopsy performed during the initial evaluation. Patients with advanced fibrosis determined by non-invasive methods should be evaluated using a second method, and if results are concordant, consider managing the same way as patients with cirrhosis.

¶ The American Association for the Study of Liver Diseases (AASLD) recommends using an ALT >30 U/L for men and >19 U/L for women as the upper limit of normal (ULN) rather than local laboratory values.

Δ Refer to UpToDate topic on "Hepatitis B virus: Overview of management" for a discussion of monitoring.

◇ Refer to UpToDate topic on "Hepatitis B virus: Overview of management" for a discussion of indications for biopsy.

§ Adefovir, lamivudine, and telbivudine are not typically used for initial treatment due to a high rate of resistance after the first year and/or weak antiviral activity.

¥ Refer to UpToDate topic on "Hepatitis B virus: Overview of management" for a discussion of which agent to use.

‡ Up to 50% of patients who achieve HBeAg seroconversion can experience a virologic relapse after discontinuing treatment with oral agents. Thus, some providers prefer to treat until HBsAg-loss.

† For most patients, antiviral therapy should be continued indefinitely. However, treatment discontinuation may be considered in persons without cirrhosis who have demonstrated loss of HBsAg. Persons who stop antiviral therapy should be monitored every month for the first 6 months.

** This includes HBeAg-positive adults with cirrhosis who seroconvert to anti-HBe on therapy.

References:

1. *Terrault NA, Bzowej NH, Chang KM, et al. AASLD guidelines for treatment of chronic hepatitis B. Hepatology. 2016 Jan; 63:261.*
2. *Lok ASF, McMahon BJ. Chronic hepatitis B: Update 2009. Hepatology 2009; 50:661. Available online at http://publish.aasld.org/Pages/Default.aspx. Accessed September 8th 2009. Copyright © 2009 American Association for the Study of Liver Diseases.*

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